

We claim:

1. A mouse comprising in its genome a first exogenous DNA molecule that functionally disrupts a NFATp gene of said mouse and a second exogenous DNA molecule that functionally disrupts a NFAT4 gene of said mouse, wherein said mouse exhibits a phenotype characterized by increased Th2 cytokine production, relative to a wildtype mouse.

2. The mouse of claim 1, wherein the phenotype of said mouse is further characterized by:

- (a) blepharitis;
- (b) interstitial pneumonitis;
- (c) splenomegaly and lymphadenopathy; and
- (d) increased levels of serum IgG1 and IgE, relative to a wildtype mouse.

3. A method of identifying a compound that regulates Th2 cell activity comprising:

a) contacting lymphoid cells deficient in NFATp and NFAT4 with a test compound; and

b) determining the effect of the test compound on an indicator of Th2 cell activity of the lymphoid cells, the test compound being identified as a modulator of Th2 cell activity based on the ability of the test compound to modulate an indicator of Th2 cell activity of the lymphoid cells deficient in NFATp and NFAT4.

4. The method of claim 3, wherein the lymphoid cells deficient in NFATp and NFAT4 are in a mouse that is deficient in NFATp and NFAT4 and the lymphoid cells are contacted with the test compound by administering the test compound to the mouse.

5. The method of claim 3, wherein the lymphoid cells deficient in NFATp and NFAT4 are isolated from a mouse deficient in NFATp and NFAT4 and the lymphoid cells are contacted with the test compound by culturing the test compound with the isolated lymphoid cells deficient in NFATp and NFAT4.

6. The method of claim 3, wherein the compound inhibits Th2 cytokine production.

7. A method of identifying a compound that regulates Th2 cell activity, comprising

a) providing at least one indicator composition comprising NFATp protein and NFAT4 protein

b) contacting the at least one indicator composition with each member of a library of test compounds;

c) selecting from the library of test compounds a compound of interest that modulates the activity of NFATp protein and NFAT4 protein; and

d) determining the effect of the compound of interest on Th2 cell activity to thereby identify a compound that regulates Th2 cell activity.

8. The method of claim 7, wherein the at least one indicator composition is at least one cell that expresses NFATp protein and NFAT4 protein.

9. The method of claim 8, wherein the at least one cell has been engineered to express NFATp protein and NFAT4 protein by introducing into the at least one cell at least one expression vector encoding the NFATp protein and the NFAT4 protein.

10. The method of claim 7, wherein the indicator composition is a cell free composition.

11. The method of claim 8, wherein the indicator composition is at least one cell that expresses an NFATp protein, an NFAT4 protein and at least one target molecule, and the ability of the test compound to modulate the interaction of the NFATp protein and the NFAT4 protein with the at least one target molecule is monitored.

12. The method of claim 8, wherein the indicator composition comprises at least one indicator cell, wherein the at least one indicator cell comprises an NFATp protein, an NFAT4 protein and at least one reporter gene responsive to the NFATp protein or the NFAT4 protein.

13. The method of claim 12, wherein the at least one indicator cell contains: at least one recombinant expression vector encoding the NFATp protein and the NFAT4 protein; and at least one vector comprising at least one NFATp- or NFAT4-responsive regulatory element operatively linked to at least one reporter gene; and said method comprises:

a) contacting the at least one indicator cell with a test compound;

b) determining the level of expression of the at least one reporter gene in the at least one indicator cell in the presence of the test compound; and

c) comparing the level of expression of the at least one reporter gene in the at least one indicator cell in the presence of the test compound with the level of expression of the at least one reporter gene in the at least one indicator cell in the absence of the test compound to

thereby select a compound of interest that modulates the activity of NFATp protein or NFAT4 protein.

5           14.    A method for modulating Th2 cell activity, comprising contacting lymphoid cells with a modulator of NFATp and NFAT4 activity such that Th2 cell activity within the lymphoid cells is modulated.

10           15.    The method of claim 14, wherein the modulator inhibits NFATp and NFAT4 activity.

15           16.    The method of claim 15, wherein the modulator is at least one antisense oligonucleotide.

20           17.    The method of claim 15, wherein the modulator is at least one intracellular antibody.

25           18.    The method of claim 15, wherein the modulator is at least one peptidic compound derived from the calcineurin-interacting region of NFATp or NFAT4.

30           19.    The method of claim 18, wherein the modulator comprises the amino acid sequence of SEQ ID NO: 1.

35           20.    The method of claim 18, wherein the peptide comprises the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 3.

            21.    The method of claim 14, wherein the modulator stimulates NFATp and NFAT4 activity.

            22.    The method of claim 21, wherein the modulator is at least one expression vector encoding NFATp and NFAT4.

            23.    The method of claim 14, wherein the lymphoid cells are contacted with the modulator by culturing the cells *in vitro* with the modulator.

35           24.    The method of claim 23, wherein the lymphoid cells are contacted with a modulator that inhibits NFATp and NFAT4 activity such that Th2 cell activity is stimulated, the method further comprising administering the lymphoid cells having increased Th2 cell activity to a subject.

25. The method of claim 14, wherein the modulator is contacted with the lymphoid cells by administering the modulator to a subject.

5 26. A method of diagnosing a subject for a disorder associated with aberrant Th2 cell activity comprising:

(a) detecting expression of NFATp and NFAT4 in lymphoid cells of a subject suspected of having a disorder associated with aberrant Th2 cell activity;

(b) comparing expression of NFATp and NFAT4 in lymphoid cells of said subject to a control that is not associated with aberrant Th2 cell activity; and

10 (c) diagnosing the subject for a disorder based a change in expression of NFATp or NFAT4 in lymphoid cells of the subject as compared to the control.

15 27. The method of claim 26, wherein expression of NFATp or NFAT4 in lymphoid cells of the subject is elevated relative to the control.

28. The method of claim 26, wherein expression of NFATp or NFAT4 in lymphoid cells of the subject is reduced relative to the control.

20 29. The method of claim 26, wherein a mutant form of NFATp or NFAT4 is expressed in lymphoid cells of the subject compared to the control.

30. The method of claim 26, wherein the expression of NFATp or NFAT4 is detected *in vivo* in the subject.

25 31. The method of claim 26, wherein the expression of NFATp or NFAT4 is detected in lymphoid cells isolated from the subject